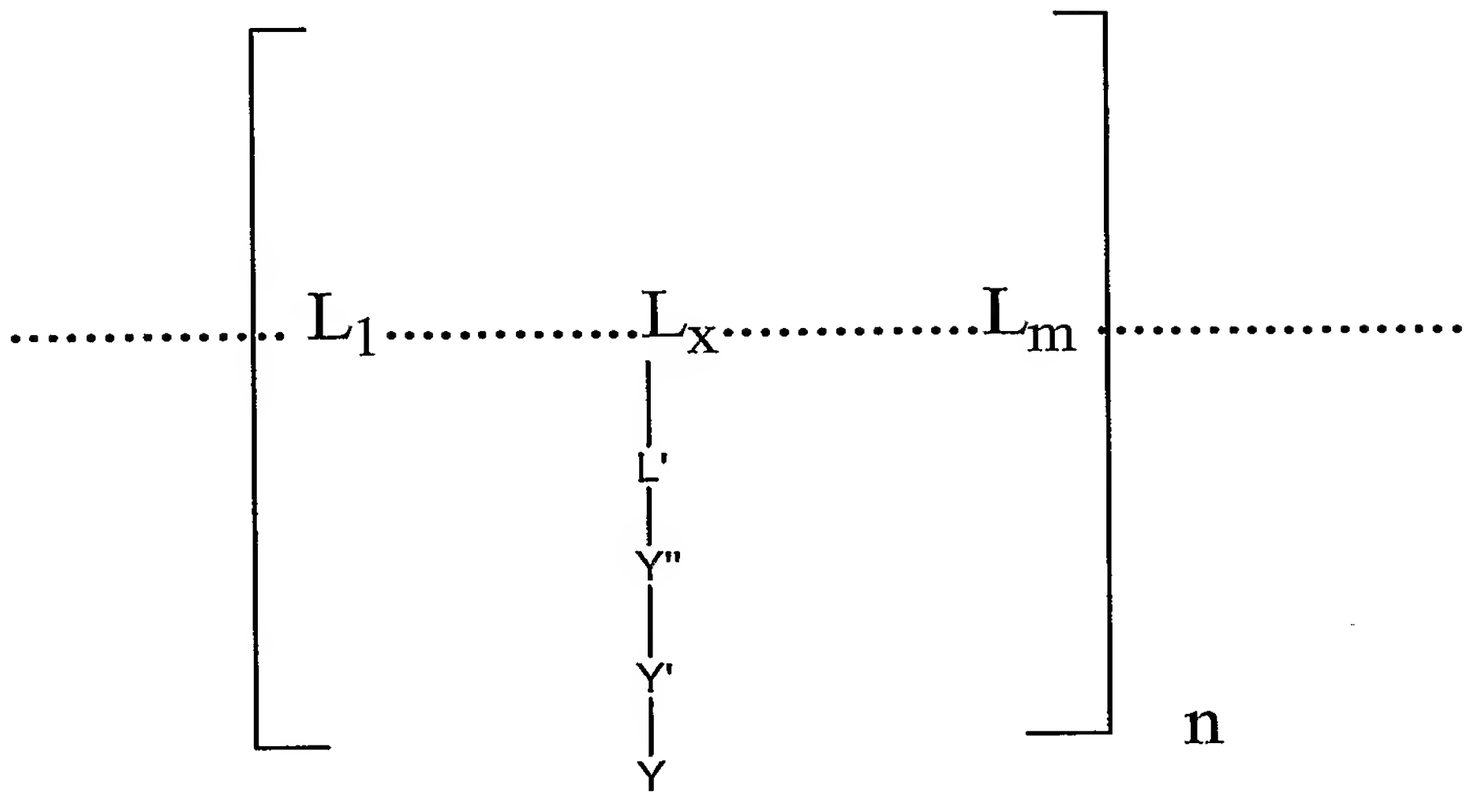
1. A covalently reactive ligand analogue (CAL) of formula (1):



(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

m is an integer from 1 to 30.

2. A CAL of Claim 1, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a

branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group or a sulfate.

3. A CAL of Claim 1, wherein L' is a side chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline.

4. A CAL of Claim 1, wherein L' is the N terminal amino group or C terminal carboxyl group of a polypeptide.

5. A CAL of Claim 1, where L' is a functional group of a ligand containing unnatural components produced by chemical conjugation or genetic engineering.

6. A CAL of claim 1 in which the ligand determinant includes DNA.

7. A CAL of claim 1 in which the ligand determinant includes RNA.

8. A CAL of claim 1 in which the ligand determinant includes a polysaccharide.

9. A CAL of claim 1 in which the ligand determinant includes a lipid.

10. The CAL of claim 1 in which Y" is a suberoyl group, a pimeroyl group, a succinyl group, an aminohexanoyl group, an aminoacetyl group, a poly(ethylene oxide)α,ω-dicarboxyl group or an acetylenedicarboxyl group

11. The CAL of claim 1 in which Y' is a charged group selected from amino(4-amidinophenyl)methyl group, 2,6-diaminopentyl group, 1-amino-4-guanidinobutyl group, 1-amino-3-carboxylpropyl group and amino(4-carboxylphenyl)methyl group.

12. The CAL of claim 1 in which Y' is a neutral group selected from amino(phenyl)methyl group, 1-amino-2-phenylethyl group, 1-amino-2-methylbutyl group, aminomethyl group, 2-aminoethyl group and 1-aminocyclohexyl group.

13. The CAL of claim 1 in which Y is composed of an electrophilic atom Z attached to one or more substituents R.

14. The CAL of claim 13 in which substituent R is an electron withdrawing group.

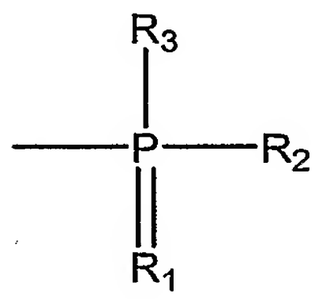
15. The CAL of claim 14 in which R is selected from phenoxyl group, 4-nitrophenoxyl group, 4-cyanophenoxyl group, pentachlorophenoxyl group, 4-nitrophenyl group, 4-cyanophenyl group, cyanomethoxyl group, trifluoromethoxyl group and 4-nitrophenylmercaptyl group .

16. The CAL of claim 13 in which R is an electron donating group.

17. The CAL of claim 16 in which R is selected from 4-methoxyphenoxyl, 4-methylphenoxyl, methoxymethoxyl, 4-methoxyphenyl, 4-methylphenyl, methoxymethyl and 4-methoxyphenylmercaptyl.

18. The CAL of claim 13 in which Z is a phosphorus, carbon, boron or vanadium atom.

19. The CAL of claim 18 in which Y has the formula (2):



(2)

in which Z is represented by a phosphorus atom,

R_1 is an oxygen or sulfur atom,

R_2 and R_3 are atoms or groups selected from hydrogen atom, oxygen atom, hydroxyl group, fluorine atom, chlorine atom, bromine atom, iodine atom, sulfur atom, sulfhydryl group, amino group, alkoxy group and phenoxy group, and

m is 4 to 22.

20. The CAL of claim 13 in which R is a glyoxylpeptide or an aminoacylpeptide.

21. A polypeptide CAL of claim 1 in which the ligand determinant ....[L_1...L_x...L_m].... is a linear poly amino acid.

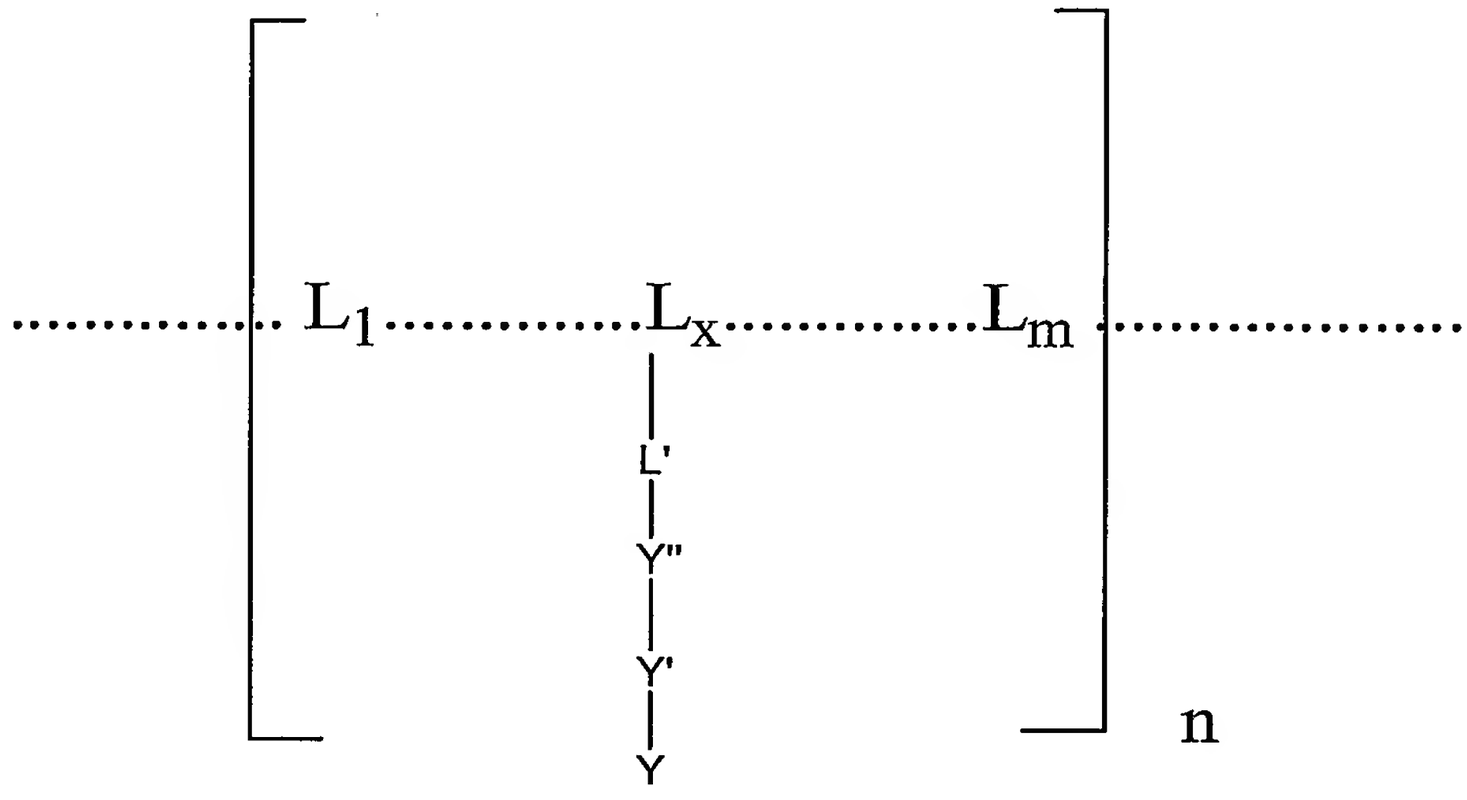
22. A polypeptide CAL of claim 1 in which the ligand determinant ....[L_1...L_x...L_m].... is a

non-linear poly amino acid.

23. A nucleic acid CAL of claim 1 in which the ligand determinant ....[L_1...L_x...L_m].... is a linear polynucleotide.

24. A nucleic acid CAL of claim 1 in which the ligand determinant ....[L_1...L_x...L_m].... is a non-linear polynucleotide.

25. A method for activating or inactivating a nucleophilic receptor (NuR), comprising: contacting a covalently reactive ligand analogue (CAL) of formula (1):



(1)

wherein, L_1...L_x...L_m are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

m is an integer from 1 to 30;

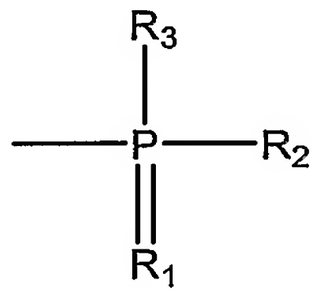
with a nucleophilic receptor that reacts specifically with the ligand determinant of said CAL.

26. The method of claim 25, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y" is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula (2):



(2)

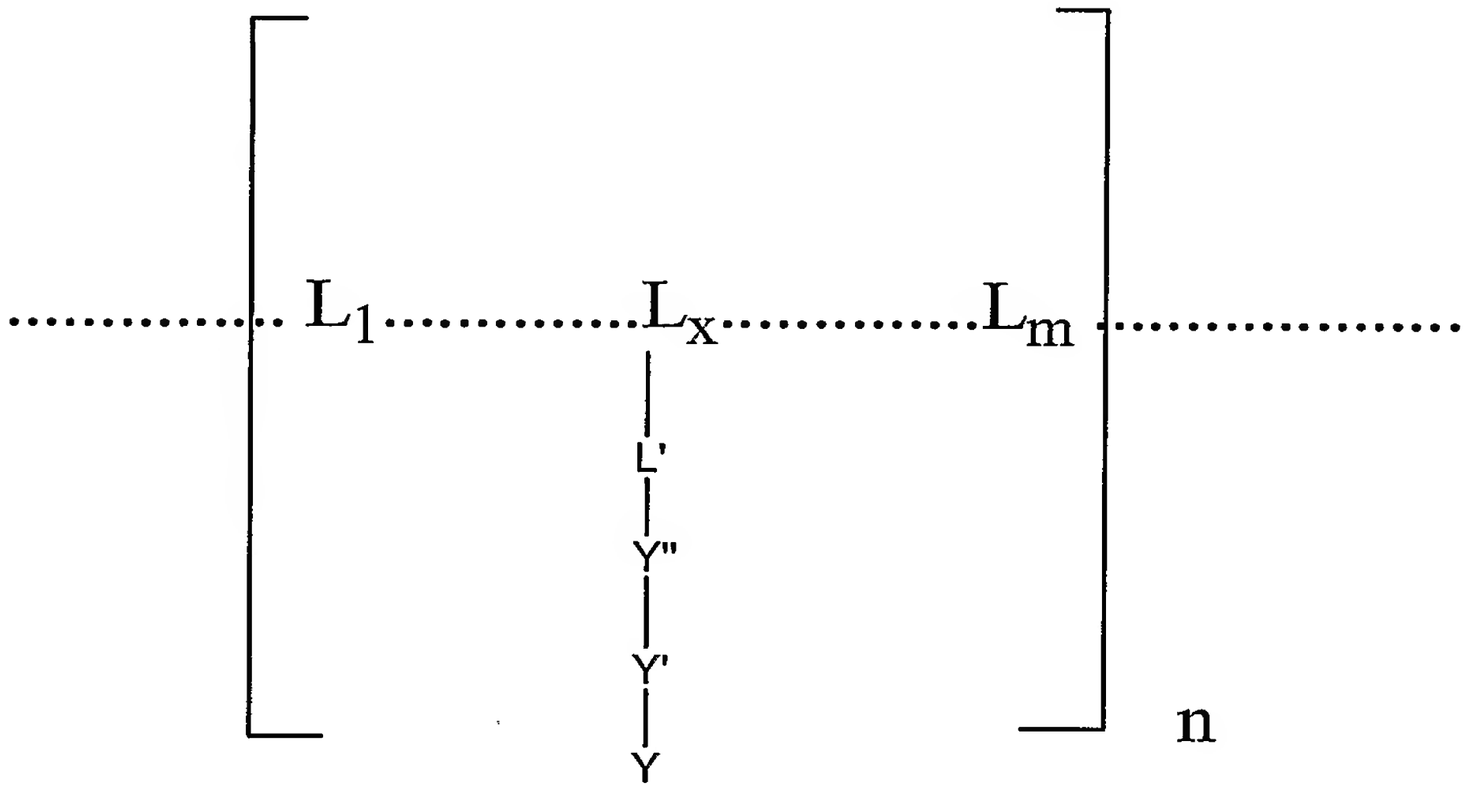
R_1 is an oxygen or sulfur atom,

R_2 and R_3 are selected from alkoxy group and phenoxy group, and

m is 4 to 22.

27. The method of claim 25, wherein the CAL is VIP-CAL, Factor VIII-CAL, β-amyloid peptide-CAL, CD4-CAL, EGFR-CAL or gp120-CAL; or the ligand is gp120, gp160, Lex1 repressor, gag, pol, hepatitis B surface antigen, bacterial exotoxins (diptheria toxin, *C. tetani* toxin, *C. botulinum* toxin, pertussis toxin.

28. A method for activating or inactivating a nucleophilic receptor (NuR) produced by a microorganism, comprising: contacting a covalently reactive ligand analogue (CAL) of formula (1):



(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

m is an integer from 1 to 30;

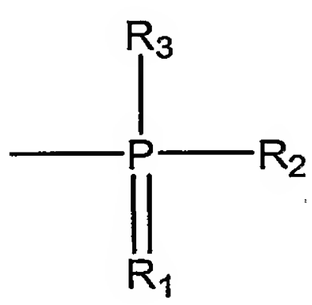
with a nucleophilic receptor produced by a microorganism, that reacts specifically with the ligand determinant of said CAL.

29. The method of claim 28, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y" is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula (2):



(2)

R_1 is an oxygen or sulfur atom,

R_2 and R_3 are selected from alkoxy group and phenoxy group, and

m is 4 to 22.

30. The method of claim 28, wherein the microorganism is a pathogen selected from HIV-1 and

HCV.

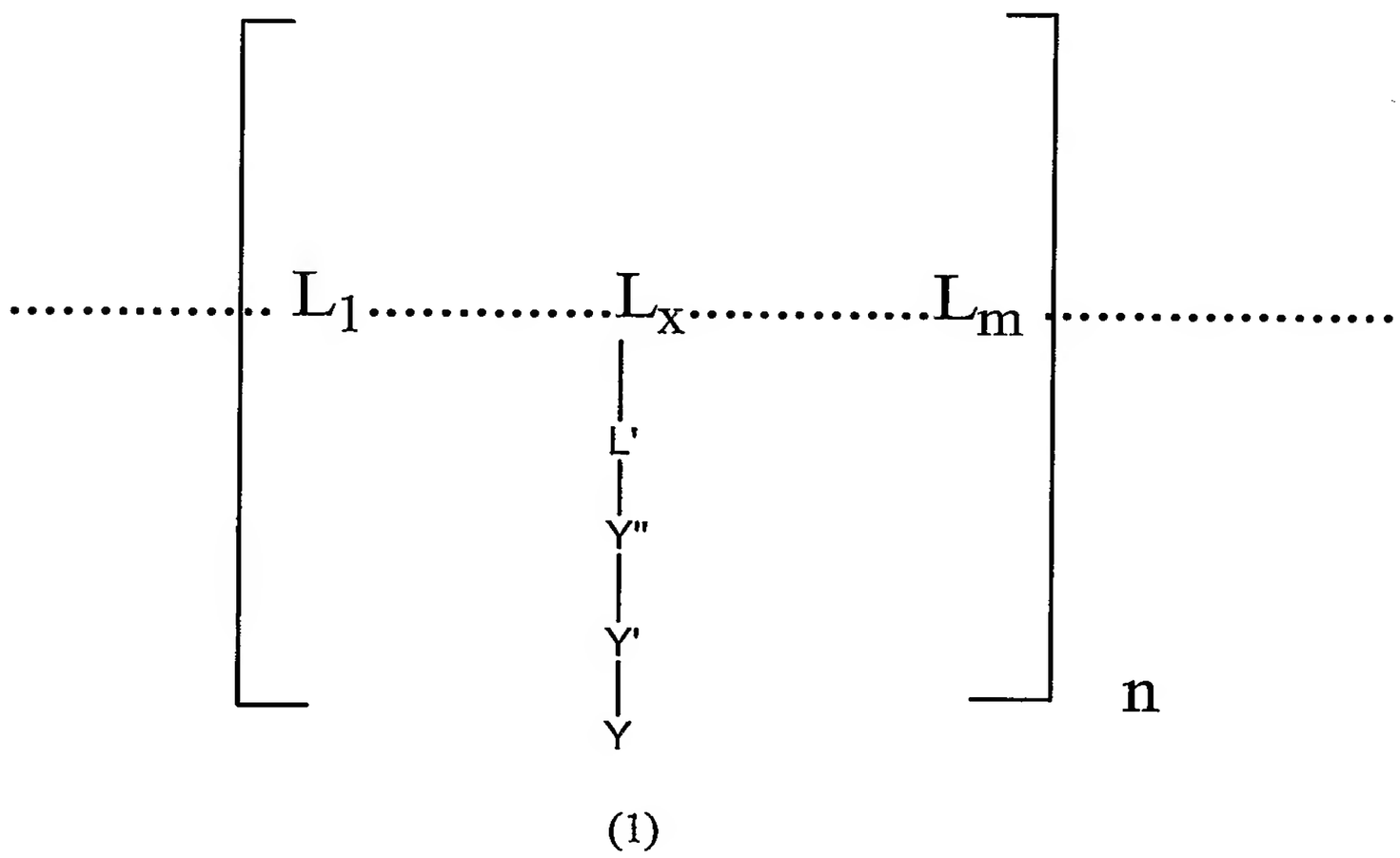
31. The method of claim 28, wherein the NuR is an antibody.

32. The method of claim 31, wherein the antibody is an autoantibody, alloantibody or xenoantibody.

33. The method of claim 31, wherein the antibody is a member of the group consisting of autoantibodies to VIP, Factor VIII Abs, thyroglobulin, prothrombin, nucleic acids, EGFR and fibrillin-1.

34. The method of claim 31, wherein the antibody is a member of the group consisting of alloantibodies to Factor VIII, red blood cell antigens, platelet antigens, kidney antigens, heart antigens and lung antigens.

35. A method for agonism or antagonism of nucleophilic receptors (NuRs) expressed on cellular surfaces, comprising: contacting a covalently reactive ligand analogue (CAL) of formula (1):



(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

m is an integer from 1 to 30;

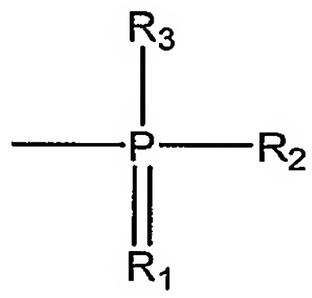
with a cell containing a NuR on its surface that reacts specifically with the ligand determinant of said CAL, resulting in activation or inactivation of cellular signal transducing system.

36. The method of claim 35, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y'' is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula (2):



(2)

R_1 is an oxygen or sulfur atom, and

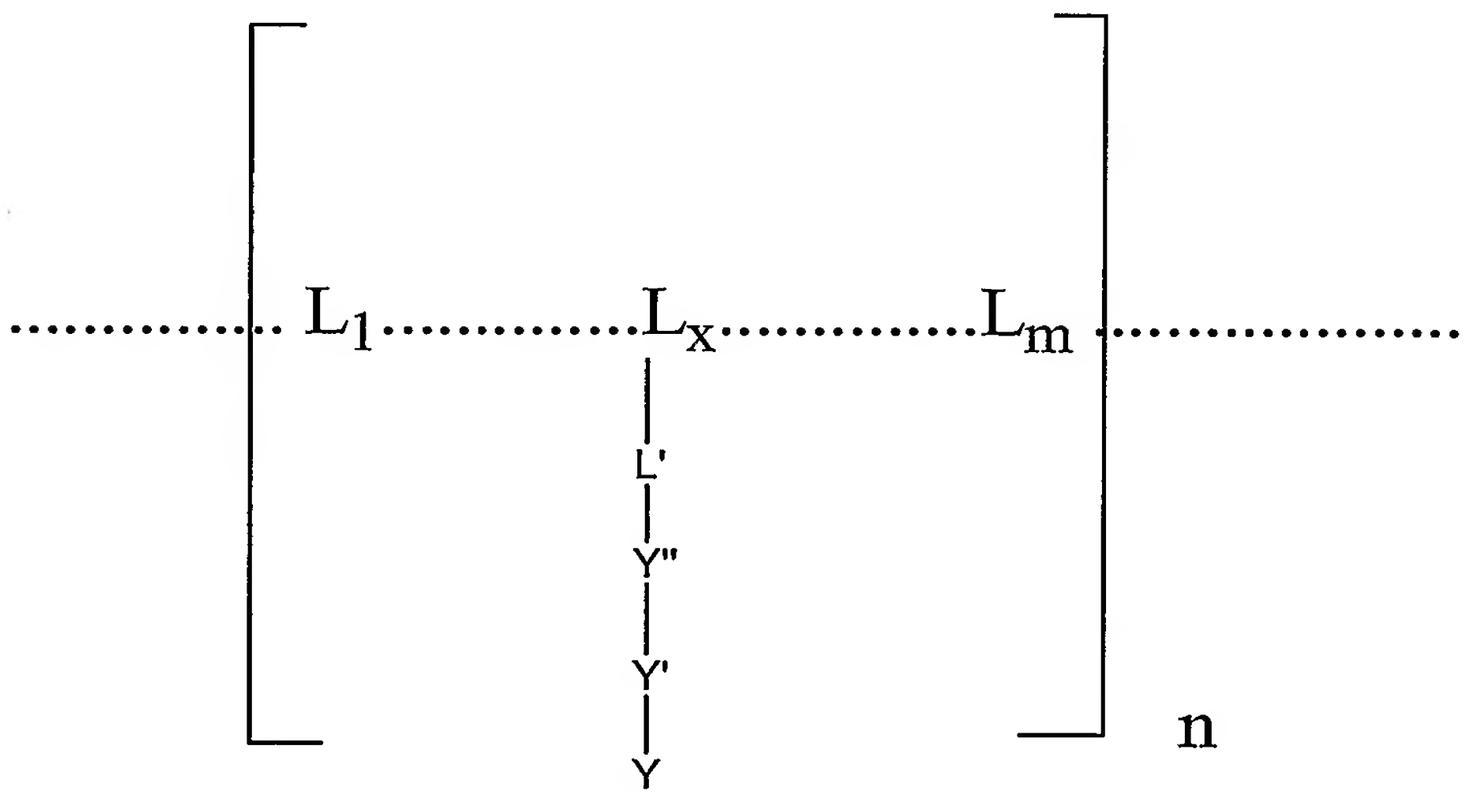
R_2 and R_3 are selected from alkoxy group and phenoxy group, and

m is 4 to 22.

37. The method of claim 35, wherein the NuR is selected from epidermal growth factor receptor, VIP receptor lymphocyte receptor, T lymphocyte receptor, growth hormone receptor and CD4.

38. The method of claim 35, wherein contact of the CAL with the NuR results in cell activation or deactivation.

39. A method for inducing growth arrest or death of cells, comprising: contacting a covalently reactive ligand analogue (CAL) of formula (1) to which a cytostatic or cytotoxic agent is optionally attached by a covalent bond:



(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

m is an integer from 1 to 30;

with lymphocytes that express NuRs which react specifically with the ligand determinant of said CAL, resulting in cellular growth arrest or death.

40. The method of claim 39 in which the cells are cancer cells.

41. The method of claim 39 in which the cells are cells infected with a microbe.

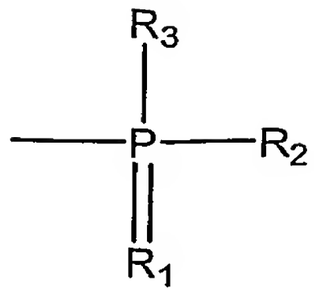
42. The method of claim 39 in which the cells are lymphocytes.

43. The method of claim 38, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y" is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula (2):



(2)

R_1 is an oxygen or sulfur atom, and

R_2 and R_3 are selected from alkoxy group and phenoxy group, and

m is 4 to 22.

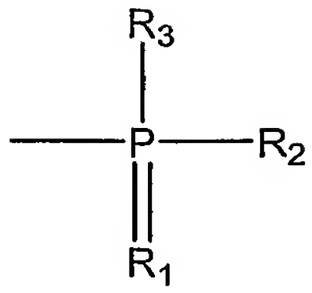
44. A method for preparing self-assembled biomolecules, comprising: subjecting a CAL of formula (1) to conditions which promote the formation of self-assembled multiple units, optionally incorporating one or more cofactor in the assembly.

45. The method of claim 44, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y" is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula (2):



(2)

R_1 is an oxygen or sulfur atom, and

R_2 and R_3 are selected from alkoxy group and phenoxy group, and

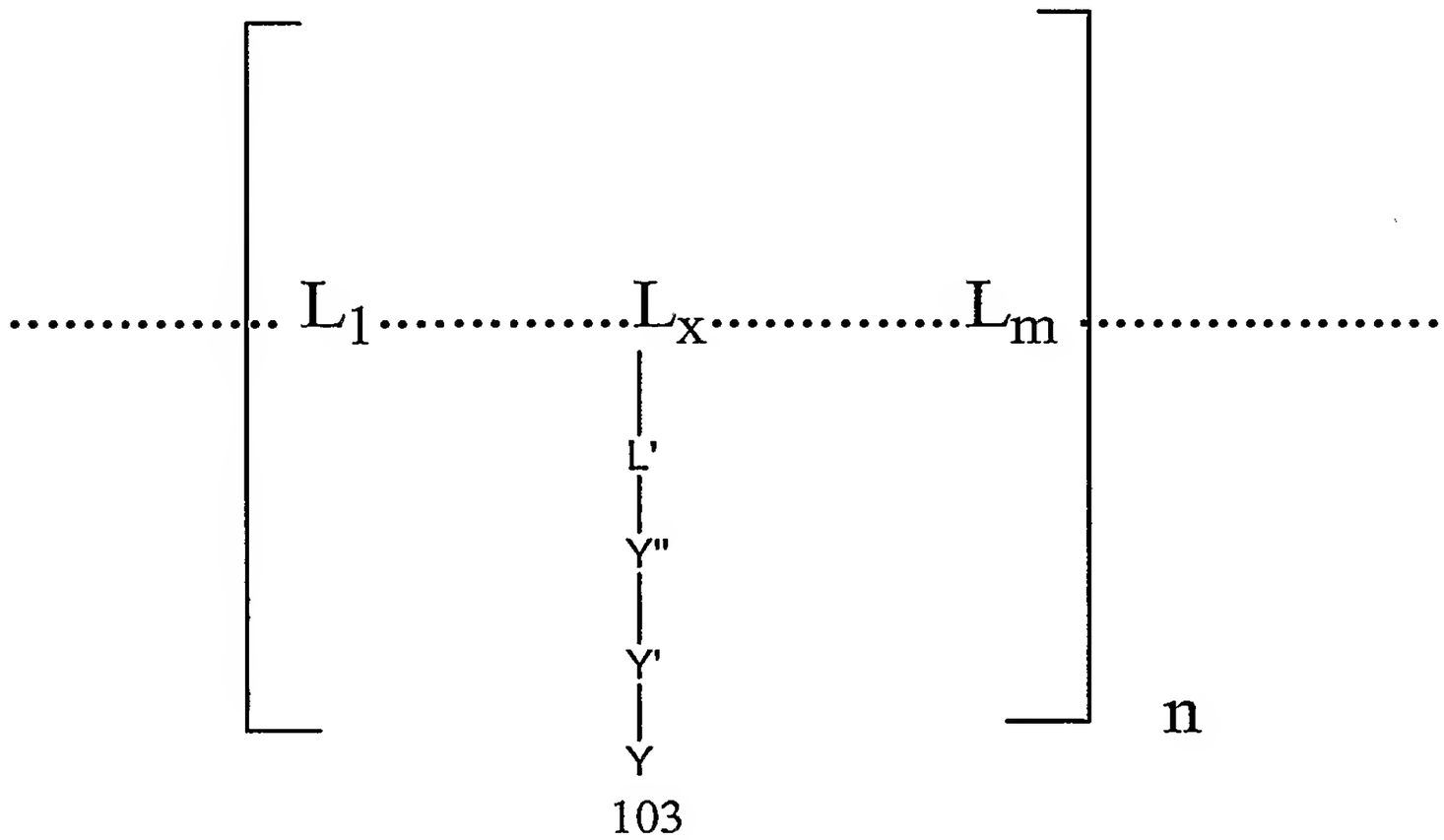
m is 4 to 22.

46. The method of claim 44, wherein the biomolecule is an oligomeric gp120-CAL.

47. The method of claim 46 in which gp41 is used a cofactor to promote the assembly of oligomeric gp120-CAL.

48. The method of claim 44, further comprising generating antibodies to said biomolecule.

49. A method of vaccination, comprising: administering to subject in need thereof an effective amount of a pharmaceutical composition containing a covalently reactive ligand analogue (CAL) of formula (1):



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(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

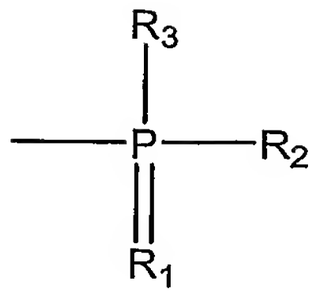
m is an integer from 1 to 30.

50. The method of claim 44, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y'' is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula ,:



(2)

R_1 is an oxygen or sulfur atom, and

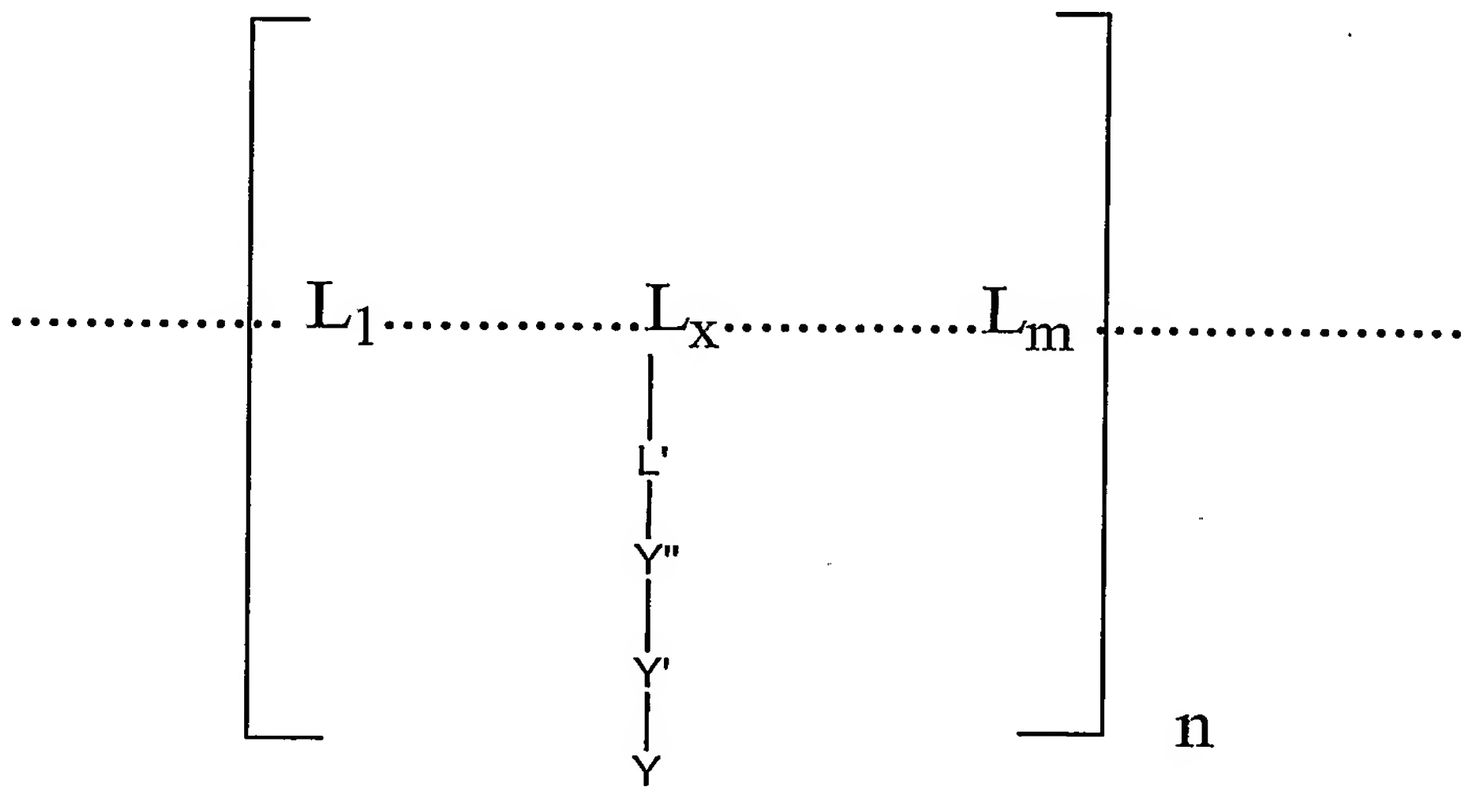
R_2 and R_3 are selected from alkoxy group and phenoxy group and

m is 4 to 22.

51. The method of claim 49, wherein the CAL is gp120-CAL.

52. The method claim 49, wherein the gp120-CAL is oligomeric gp120-CAL.

53. A method for passive immunotherapy, comprising: administering to a subject in need thereof an effective amount of a pharmaceutical composition containing antibodies that bind to a covalently reactive ligand analogue (CAL) of formula (1):



(1)

wherein, $L_1 \ldots L_x \ldots L_m$ are components defining a ligand determinant,

L_x is a component unit of the ligand determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide,

L' is a functional group of L_x,

Y'' is atom, covalent bond or linker,

Y' is an optional charged or neutral group

Y is a covalently reactive electrophilic group that reacts specifically with a receptor that binds to said ligand determinant, and

n is an integer from 1 to 1000

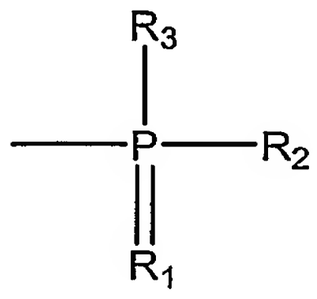
m is an integer from 1 to 30.

54. The method of claim 53, wherein L' is selected from a carboxyl group, an amino group, a hydroxyl group, a sulfhydryl group, a 4-hydroxy phenyl group, a phenyl group, an imidazole group, an indole group, a methylthioethyl group, a guanidino group, a linear alkyl group, a branched alkyl group, a cyclic alkyl group, a linear alkenyl group, a branched alkenyl group, a cyclic alkenyl group, a linear alkynyl group, a branched alkynyl group, an cyclic alkynyl group, an aryl group, an amide group, an aldehyde group, a ketone group, a phosphate group, a sulfate group, or a chain functional group of the following amino acid residues: glycine, alanine, leucine, isoleucine, valine, methionine, cystein, aspartic acid, glutamic acid, asparagine, glutamine, lysine, arginine, phenylalanine, tyrosine, tryptophan, histidine, serine, threonine or proline,

Y'' is a suberoyl group,

Y' is an amino(4-amidinophenyl)methyl group or an amino(phenyl)methyl group,

Y has the formula ,:



(2)

R_1 is an oxygen or sulfur atom, and

R_2 and R_3 are selected from alkoxy group and phenoxy group and

m is 4 to 22.

55. The method of claim 53, wherein the antibodies are monoclonal antibodies or mixtures of antibodies directed to oligomeric gp120-CAL.

56. A method for imaging, comprising: exposing cells or tissues which express a NuR on the cell surfaces to a detectably labeled derivative of a CAL of formula (1), and detecting the label.

57. The method of claim 56, when imaging tumor tissue, tumor cells, infected tissue or infected cells.

58. A method for producing receptors or enzymes having improved ligand binding or enzymatic activity, comprising: subjecting a receptor or an enzyme to directed evolution or a mutation process, and isolating a receptor or enzyme with improved ligand binding or enzymatic activity, by contacting it with a CAL of formula (1).

59. The method of claim 58, wherein the resulting protein is derived from growth hormone receptor, VIP receptor, trypsin, chymotrypsin, thrombin, subtilisin, or an antibody to HIV-1.

60. An immunoassay for detection of antibodies or antigens, comprising: contacting an immobilized CAL of formula (1) or a detectably labeled CAL of formula (1).

61. The immunoassay of claim 60, for detecting HIV or HCV.